

***Remarks***

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 1, 4-10, 20, 22, 23, 25, 26, 54, 57-65, 68-74, and 79-101 are pending in the application, with claim 1 being the independent claim. Claims 2, 3, 11-19, 21, 24, 27-53, 55, 56, 66, 67 and 75-78 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein and new claims 93-101 are sought to be added.

The claims have been amended to limit the compounds to 4-*H*-pyrrolo[2,3-*h*]chromes and R<sub>1</sub> to methyl, hydroxymethyl, and an ester thereof. Support for this amendment and for new claims 93-101 may be found in canceled claims 3 and 12 and in paragraph [0044] of the as-filed application which describes esters of hydroxy-containing compounds as prodrugs. In addition, the claims have been amended to delete reference to individual compounds wherein R<sub>1</sub> is other than methyl, hydroxymethyl or an ester thereof and to correct several obvious typographical errors. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***The Restriction Requirement***

Applicants acknowledge with appreciation the regrouping of the claims in the present Office Action. Upon allowance of the elected compound claims, Applicants

respectfully request that the examiner rejoin method claims 65, 68-74, 79-92 and new claims 97, 98 and 101 to the elected claims.

***Rejections under 35 U.S.C. § 102***

Claims 1-9, 11-19, 21-23, 54 and 57-64 are rejected under 35 U.S.C. § 102(a) as being anticipated by Drewe, J.A. *et al.*, WO 2001/034591 (hereinafter "Drewe"). Office Action, page 5, numbered paragraph 4.

It is the Examiner's opinion that Drewe teaches some of the same compounds as the present application. Applicants respectfully traverse this rejection.

Drewe does not teach the 4*H*-pyrrolo[2,3-*h*]chromenes of the present invention where R<sub>1</sub> is methyl, hydroxymethyl or an ester thereof. Therefore, Drewe does not anticipate the claimed invention. Withdrawal of the rejection is respectfully requested.

Claims 1-9, 11-19, 21-23, 54 and 57-64 are provisionally rejected under 35 U.S.C. § 102(e) as being anticipated by copending Application No. 11/150,586 (hereinafter "the '586 application"). Office Action, page 7, numbered paragraph 5.

It is the Examiner's opinion that the '586 application contains some of the same compounds as in the present application. Applicants respectfully traverse this rejection.

The '586 application does not teach the 4*H*-pyrrolo[2,3-*h*]chromenes of the present invention where R<sub>1</sub> is methyl, hydroxymethyl or an ester thereof. Therefore, the '586 application does not anticipate the claimed invention. Withdrawal of the rejection is respectfully requested.

Claims 1-26, 54 and 57-64 are provisionally rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 7,053,117 (hereinafter "the '117 patent"). Office Action, page 9, numbered paragraph 6.

It is the Examiner's opinion that the '117 patent contains certain of the same compounds as in the present application. Applicants respectfully traverse this rejection.

The '117 patent does not teach the 4*H*-pyrrolo[2,3-*h*]chromenes of the present invention where R<sub>1</sub> is methyl, hydroxymethyl or an ester thereof. Therefore, the '117 patent does not anticipate the claimed invention. Withdrawal of the rejection is respectfully requested.

Claims 1-9, 11-19, 21-23, 54 and 57-64 are rejected under 35 U.S.C. § 102(e) as being anticipated by Drewe and U.S. Patent No. 7,015,328 (hereinafter "the '328 patent"). Office Action, page 10, numbered paragraph 7.

The '328 patent does not teach the 4*H*-pyrrolo[2,3-*h*]chromenes of the present invention where R<sub>1</sub> is methyl, hydroxymethyl or an ester thereof. Therefore, the '328 patent does not anticipate the claimed invention. Withdrawal of the rejection is respectfully requested.

#### ***Obvious-Type Double Patenting Rejections***

Claims 1-40, 54 and 57-64 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 48-51 and 54-81 of co-pending Application No. 10/514,426 (hereinafter "the '426 application"). Office Action, page 11, numbered paragraph 8. Applicants respectfully traverse this rejection.

The Examiner states that the conflicting claims are not identical, but they are not patently distinct from each other because they contain the same compounds and compositions. Applicants respectfully disagree. The claims of the '426 application do not recite the 4*H*-pyrrolo[2,3-*h*]chromenes of the present invention where R<sub>1</sub> is methyl, hydroxymethyl or an ester thereof.

Applicants respectfully direct the attention of the Examiner to the data set forth in Example 44 showing that 4*H*-pyrrolo[2,3-*h*]chromenes having R<sub>1</sub> = methyl and hydroxymethyl have unexpectedly better potency in an assay for caspase activation. As described on pages 1-4 of the present specification, compounds which activate caspase enzymes are useful for the treatment of cancer. Therefore, the claims of the present application are clearly not obvious in view of the claims of the '426 application.

Withdrawal of the rejection is respectfully requested.

Claims 1-40, 54 and 57-64 are also provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 17-9 [sic, 17-19], 29, 30, 32, 61 and 57 of copending Application No. 11/150,586 (hereinafter "the '586 application"). Office Action, page 12, numbered paragraph 9. Applicants respectfully traverse this rejection.

The Examiner states that the conflicting claims are not identical, but they are not patently distinct from each other because they contain the same compounds and compositions. Applicants respectfully disagree. Applicants first note that the elected claims of the present application are compound and composition claims while the claims of the '586 application are method claims. Moreover, the claims of the '586 application do not recite the 4*H*-pyrrolo[2,3-*h*]chromenes of the present invention where R<sub>1</sub> is

methyl, hydroxymethyl or an ester thereof. Therefore, the claims of the present application are clearly not obvious in view of the claims of the '586 application. Withdrawal of the rejection is respectfully requested.

Claims 1-40, 54 and 57-64 are also provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 41-63 and 73-78 of copending Application No. 11/072,499 (hereinafter "the '499 application"). Office Action, page 12, numbered paragraph 10. Applicants respectfully traverse this rejection.

The Examiner states that the conflicting claims are not identical, but they are not patently distinct from each other because they contain the same compounds and compositions. Applicants respectfully disagree. The claims of the '499 application do not recite the 4*H*-pyrrolo[2,3-*h*]chromenes of the present invention where R<sub>1</sub> is methyl, hydroxymethyl or an ester thereof. Therefore, the claims of the present application are clearly not obvious in view of the claims of the '499 application. Withdrawal of the rejection is respectfully requested.

***Rejections under 35 U.S.C. § 112***

Claims 1-40, 54 and 57-64 are rejected under 35 U.S.C. § 112, first paragraph, for nonenablement. Office Action, page 13, numbered paragraph 11. Applicants respectfully traverse this rejection.

The Examiner has based this rejection upon the limited number of heteroaryl aldehyde starting materials which are available from Sigma. Applicants respectfully disagree. Attached please find the results of a similar search for commercially available

heteroarylaldehydes in SciFinder. The results show that 543 such compounds are available. In addition, one of ordinary skill in the art is not limited to commercially available compounds. Enablement can also be provided by the knowledge in the art concerning the synthesis of heteroarylaldehydes. Thus, this basis for the rejection is clearly in error.

The Examiner has also based this rejection upon the report by Kemnitzer *et al.*, *J. Med. Chem.* 47:6299-6310 (2004) which indicates that the identity of the group in the 4-position for some related compounds, is critical for activity. Again, Applicants respectfully direct the attention of the Examiner to Example 44 which shows that compounds having a 7-methyl substituent and various A groups have very high caspase activation activity.

Moreover, just because a compound may have a lower caspase activation activity does not mean that the compound will be ineffective in inhibiting tumor growth.

The Examiner also notes that certain benzopyrans are carcinogens. Applicants submit that this assertion has no relevance to the present invention as the claimed compounds are pyrrolo[2,3-*h*]chromenes and not benzopyrans. Furthermore, it is the responsibility of the U.S. Food and Drug Administration to regulate the safety and effectiveness of drugs, not the U.S. Patent and Trademark Office. The hypothetical carcinogenic activity of the claimed compounds is not an adequate basis to find that the claimed invention is not enabled.

In view of Applicants' presumptively enabled disclosure and the evidence submitted herewith, Applicants submit that the Examiner has not provided a sound scientific basis for concluding that the present invention is not enabled.

***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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